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Title: Lung function, weight, and sweat chloride responses in patients with cystic fibrosis and the G551D-CFTR mutation treated with ivacaftor: A secondary analysis

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Body: Clinical studies show improved FEV₁ in ivacaftor-treated CF patients with the G551D-CFTR mutation when compared with placebo. To better understand the clinical benefit for those who fall below the median response, we examined pharmacodynamic and efficacy data from Phase 3 ivacaftor Studies 102/103. This secondary analysis of patients who received 48 weeks of ivacaftor (n=109) or placebo (n=100), examined the number needed to treat (NNT), frequency and cumulative distribution functions and subset analyses to evaluate response (sweat chloride, FEV₁, weight). Changes in these outcomes according to FEV₁ response were also compared. The NNT for a reduction in sweat chloride of 20 mMol/L was 1.03. To achieve an improvement in FEV₁ of ≥5%, NNT was 1.73. For both treatment populations, the data were normally distributed with a shift toward benefit for the ivacaftor group. Numerical differences were seen in sweat chloride and weight for ivacaftor-treated patients, regardless of whether or not a ≥5% FEV₁ improvement was achieved (Table). Ivacaftor was observed to produce an effect on sweat chloride, FEV₁, and weight. These analyses indicate that in % predicted FEV₁ responders (>5% improvement) and minimal responders (<5% improvement) weight gain and change in sweat chloride are similar.